REMARKS

These remarks are in response to the Final Office Action mailed March 15, 2004. Claims 26, 29-32, 34, 37-40, 42, 44-46 and 50 are allowed. Applicants have amended Figures 1A, 1B, 2, and 3 to delete the figure legends associated with each. If the Examiner would like to discuss any of the issues raised in the Office Action, Applicants' representative can be reached at (858) 678-5070.

Please charge any fees, or make any credits, to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 5/14/04

Michael Reed
Reg. No. 45,647

Fish & Richardson P.C.
PTO Customer No. 20985
12390 El Camino Real
San Diego, California 92130
Telephone: (858) 678-5070
Facsimile: (858) 678-5099

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FIGURE 1A

20CAGHA

CTGCAGGCCAGCGTCCTGATAAGTGAATTC*GCCGCCACC*ATGGGAGGCCCAC
CGTCAACCCCCCAGCAGCAGCAACAGCAGCAGCAACAGCAACAGCAGCAGC
AACAACAGCAGCAGCAACAGACTAGTCGTACGTATCCCTATGACGTGCCCGA
CTATGCGTAG

127CAGHA

CTGCAGGCCAGCGTCCTGATAAGTGAATTC*GCCGCCACC*ATGGGAGGCCCAC
CGTCAACCCCCCAGCAGCAGCAACAGCAGCAGCAACAGCAACAGCAGCAGC
AACAACAGCAGCAGCAACAGCAACAGCAGCAGCAACAACAGCAGCAGCAAC
AGCAACAGCAGCAGCAACAGCAGCAGCAACAGCAACAGCAGCAGCAACAAC
AGCAGCAGCAACAGCAACAGCAGCAGCAACAACAGCAACAACAACAGCAAC
AGCAGCAGCAACAGCAGCAGCAACAGCAACAGCAGCAGCAACAACAGCAGC
AGCAACAGCAACAGCAGCAGCAACAACAGCAGCAGCAACAGCAACAGCAGC
AGCAACAGCAGCAGCAACAGCAACAGCAGCAGCAACAACAGCAGCTGCAAC
AGCAACAGCAGCAGCAACAACAGCAGCAGCAACAGACTAGTCGTACGTATC
CCTATGACGTGCCCGACTATGCGTAG

FIGURE 1B

20QHA

MGGPPSTPQ$_{20}$TSRTYPYDVPDYA

127QHA

MGGPPSTPQ$_{127}$TSRTYPYDVPDYA

~~Figure 1. A) DNA sequences of 20QHA and 127QHA and B) their predicted protein sequences. The protein coding region is underlined. The Kozak sequence is in italic.~~

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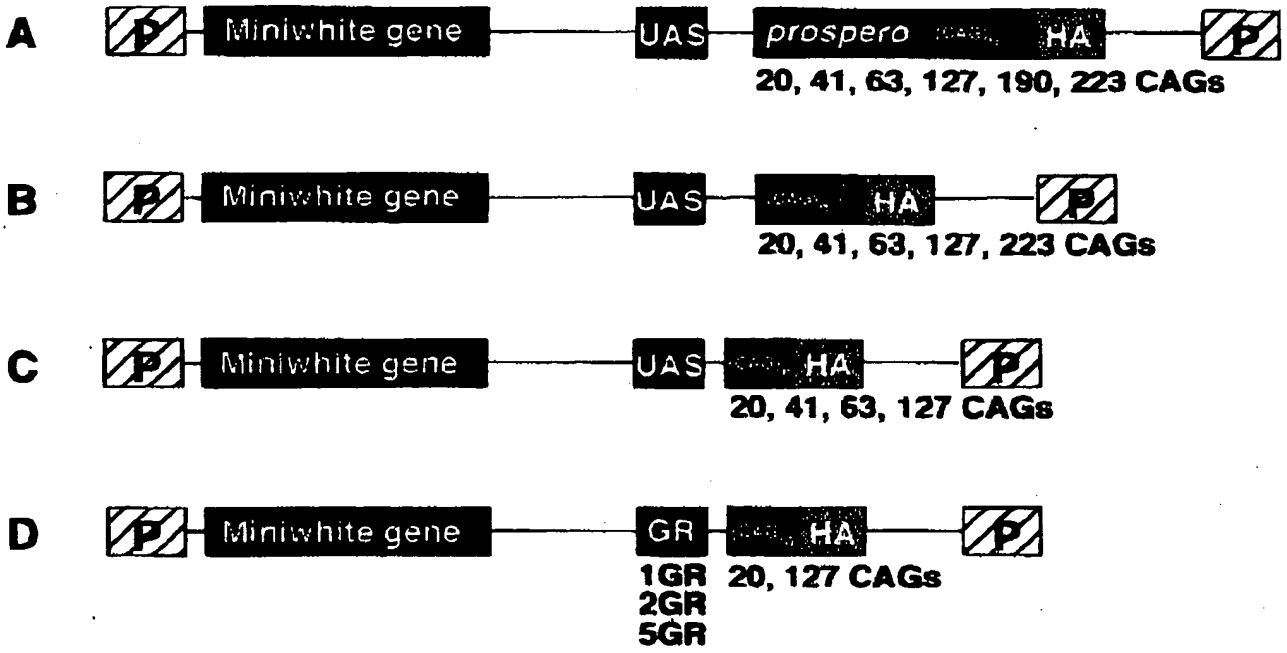
FIGURE 2



~~Figure 1. P-element plasmid constructs for production of transgenic flies.~~ Each construct has two P-elements for chromosomal insertion. To facilitate identification of transformed flies, a miniwhite gene is included to produce red pigmentation in the eye. **A)** Plasmids carrying the full-length cDNA encoding the fly PROSPERO with various CAG repeat sizes. The expression of PROSPERO is regulated by five tandem upstream activating sequences (UAS). The yeast transcription factor GAL4 activates the transcription from these UAS elements. At its 3'-end, *prospero* cDNA is joined, in-frame, to a short DNA sequence that codes for a heterologous epitope, hemeagglutinin (HA). Antibodies against HA will be used to label the protein in immunohistochemical assays and Western blots. **B)** Plasmids carrying a partial cDNA encoding 422 amino acids of the C-terminal end of PROSPERO with various CAG repeat sizes. **C)** Plasmids carrying a DNA sequence that only encodes polyglutamines of various sizes. **D)** Plasmids carrying a DNA sequence that only encodes polyglutamines of various sizes, expressed under the control of one, two or five GLASS response elements (1GR, 2GR, or 5GR). The eye-specific protein GLASS activates the ~~expression of polyglutamines from the GLASS response elements.~~

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FIGURE 3

Generation of the P-element insertion and screening for modifiers

M P[Δ2-3]/P[Δ2-3] **X** **F** EP55/EP55

↓

M EP55/Y;; P[Δ2-3]/+ **X** **F** w/w

↓

M w/Y;pEP/+;+ **or** w/Y;+;pEP/+ **X** **F** w;GMR/CyO;127Q/127Q

↓

Progeny screened for eye phenotype

Isolation of the new P-element insertion (pEP = suppressor or enhancer)

M (GMR;127Q)/pEP **X** **F** (CyO;TM3)/Xa

↓

M GMR/CyO;pEP/TM3 **X** **F** w1118

↓

M GMR;TM3 or CyO;pEP **X** **F** w;GMR/CyO;127Q/127Q to test

X **F** (CyO;TM3)/Xa to establish line

↓

M +/CyO;pEP/TM3 **X** **F** +/CyO;pEP/TM3

↓

pEP/TM3 or pEP/pEP established lines

~~Genetic scheme used for generating P-element mutants, screening for modifiers~~ of polyglutamine toxicity, and isolating a hypothetical modifier P-element insertion on chromosome 3. Homozygous EP55 virgin females were crossed with males homozygous for a defective transposon, expressing the transposase. The F1 male progeny were crossed with virgin *w1118* females. The F2 Male progeny that had coloured eyes and lacked the transposon's genetic markers were selected, as they contain a new stable insertion on an autosomal chromosome. These males were crossed with flies heterozygous for GMR-GAL4 on chromosome 2, balanced by CyO chromosome, and homozygous for UAS-127Q on chromosome 3. The resulting F3 progeny were screened for eye phenotype. Once a modifier was found, a single male was crossed to female (CyO;TM3)/Xa. The resulting male progeny were crossed to *w1118* flies to separate the P-elements. This resulted in colored-eye progeny that carry a balancer for one chromosome and a P-element on another. Males from such progeny were tested for modifier activity by crossing to female w;GMR/CyO;127Q/127Q. The lines were established by crossing the latter males to (CyO;TM3)/Xa, and by crossing the resulting flies carrying CyO and TM3 balancers. **EP55**: source of transposable P-element; **P[Δ2-3]**: source of transposase; **F**: female; **M**: male; **CyO**: balancer chromosome 2; **TM3**: balancer chromosome 3. **Xa**: ~~translocation (2;3) Xa. (Chromosome 4 is omitted.)~~